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EFFECT OF PREDNISONE AND CORTISONE ON THE SUPRARENAL GLANDS OF RATS

BY

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Effect of prednisone and cortisone on the suprarenal glands of rats

by

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Increasing attention is being paid in clinical therapy and experimental research to the side-effects of cortisone. Numerous clinical and experimental studies have been carried out in which atrophy of the suprarenal body has been observed in connection with the administration of cortisone. A further drawback in the application of cortisone therapy is the retention of, e.g., Na^+ and Cl^- as well as the excretion of K^+. This causes an increase in the amount of extra-cellular water, which becomes evident in a tendency to edema among patients thus treated.

Recently a new synthetic cortisone derivative, prednisone, has been developed, and, correspondingly, a hydrocortisone derivative, prednisolone. These differ from cortisone and hydrocortisone only in the respect that in the molecule there exists additional double bond in the position 1, 2. Their physiological effects differs considerably, however, from that of cortisone and hydrocortisone. In tests on human beings it has been observed that prednisone has little effects on the balance of Na^+, Cl^- and K^+ (1, 2, 6, 4). During the performance of the tests the 17-ketosteroids are observed to decrease, while after the discontinuation of treatment they again rise to the normal level (1, 2, 5, 7). Very soon after the administration of prednisone, eosinopenia may be observed to exceed four to five times that following a corresponding cortisone dose (1, 2, 6, 4, 7).

Prednisone dosages are prescribed for laboratory animals by using as criterion the anti-inflammatoric and eosinopenic effect and the involutionary effect on the lymphatic tissue. It has been noted that a cortisone dose of comparable effect has to be four to five times as large as the dose of prednisone.

As in cortisone therapy, there apparently occurs atrophy of the suprarenal cortex in connection with prednisone therapy. We have not, however, been able to find any detailed report on this matter in the literature. In one study (3), carried out with cortisone, hydrocortisone and prednisone, all three drugs are observed to have the same kind of eosinopenic effect.

The purpose of our investigation was to compare by weighing and histologically studying, the atrophic action of cortisone and prednisone doses of equal clinical effect on the suprarenal body of the rat.

The laboratory animals used were 45 male rats. They ranged in weight from 140 to 200 g, and they were divided into three groups of equal size. One group was used as a control series and the animals belonging to it received an 0.5 cc daily injection of physiological NaCl-solution. The other group received 5 mg of cortisone acetate suspended in 0.5 cc of physiological NaCl-solution. The third group received 1.25 mg of prednisone in the same amount of liquid. The injections were given subcutaneously daily for fourteen days. The animals were killed on the fifteenth day from the start of the experiment by being shot in the head. Immediately thereafter both suprarenal glands were weighed in a torsion balance. After this they were fixed in 5 % formaline. Twenty-four hours later a section (15μ) was cut with the freezing microtome and immediately afterward the sections were stained with Sudan III. The preparations were examined microscopically and photographed immediately after staining.

RESULTS

No very great differences between the different groups of animals could be observed during the experiment. All the animals remained alive throughout the period. The rats receiving cortisone were shaggy haired and their movements were slow compared to those of the control animals. The animals given prednisone differed very little in this respect from the members of the control group.

Weights of the suprarenal glands: The weights are presented in Figure 1. The weights were compared with each other by means of the t-test. The means of the control and prednisone groups ($\bar{x}_o = 18.8$, $\bar{x}_p = 15.2$) deviate from each other quite significantly ($t = 4.14^{+++}$). Likewise do the means in the prednisone and cortisone groups ($\bar{x}_p = 15.2$, $\bar{x}_c = 11.5$) quite significantly deviate from each other ($t = 3.96^{+++}$).

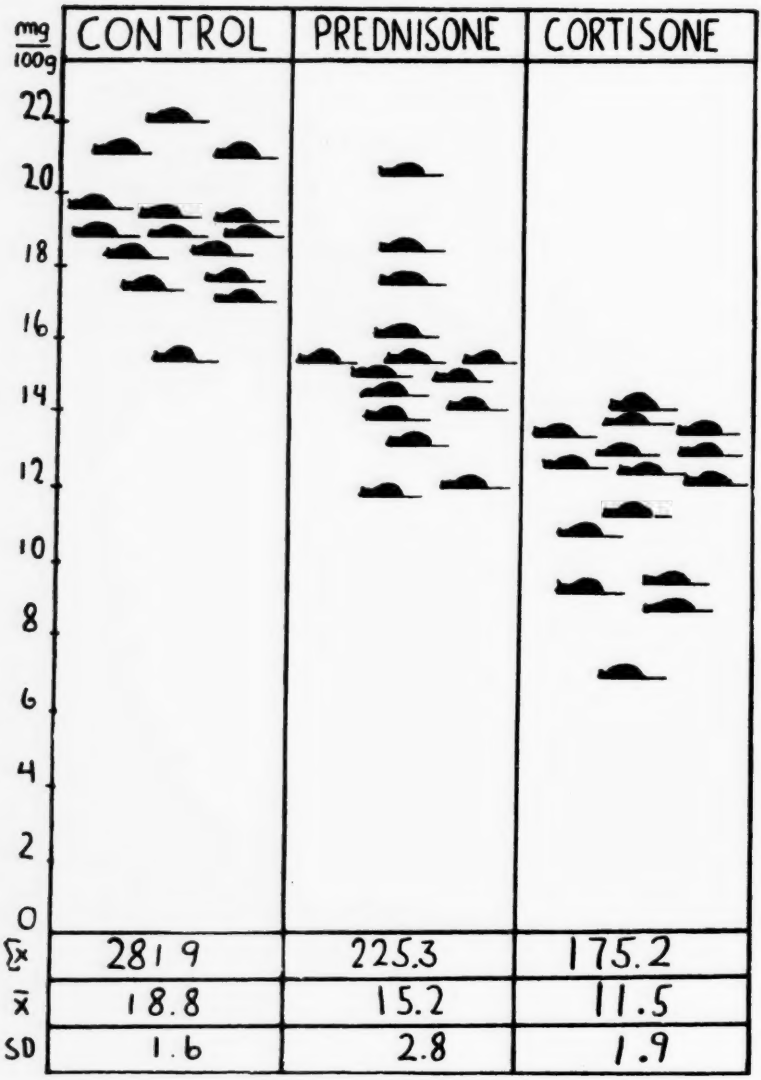
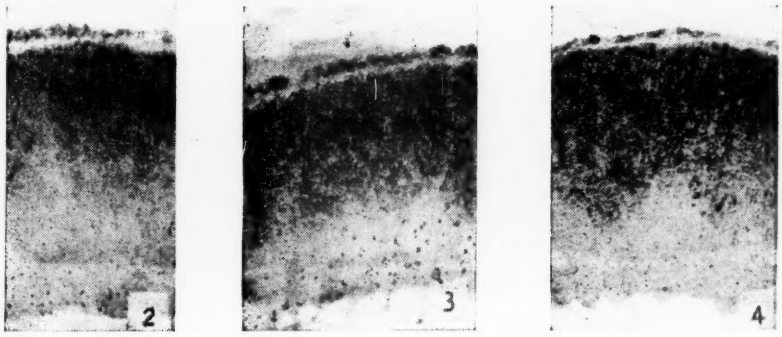


Fig. 1. — The aggregate weight of the suprarenal glands of the laboratory animals per 100 g of body weight. Σx = sum of foregoing values. $\bar{x}$ = their mean. SD = standard deviation.

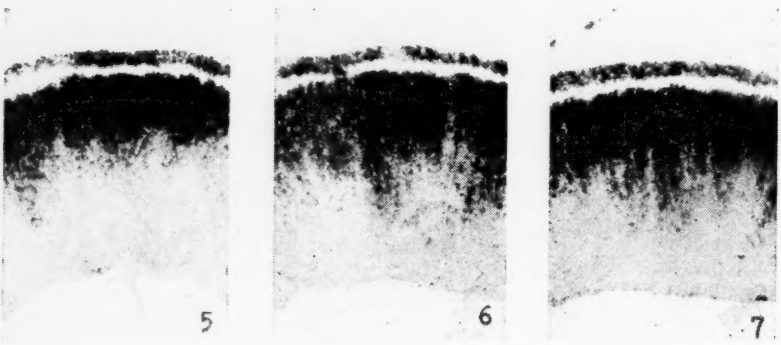
Sudan Staining

Control group. — The zona glomerulosa exhibits a fair abundance of sudanophilic drops. The stain is not evenly distributed, but weakly stained areas are met with here and there. In all the control animals there is a sudanophobic zone, the width of which varies little from animal to animal. The outer layer of the fascicular zone is more strongly and more evenly stained than the inner part, where varying sudanophilic drops are found. Sudanophilic drops occur only in places in the reticular zone. The size of the drops does not vary appreciably in the different layers. (Figs. 2, 3 and 4.)



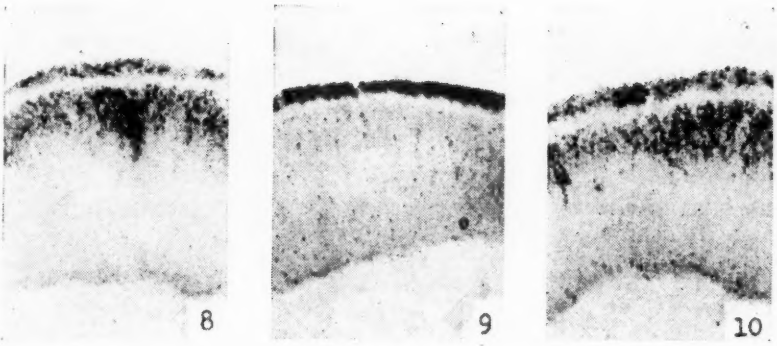
Figs. 2, 3 and 4. — Control group, Sudan staining. About 50 x.

Prednisone group. — No deviation is to be observed in the glomerular zone upon comparison with the control animals. A sudanophobic zone is to be seen in all the preparations. The outer part of the fascicular zone stains as in the case of the control rats, but the sudanophilic area is, in general narrower. The zona reticularis resembles that of the controls. The thickness of the cortex is, on the whole, somewhat smaller than in the case of the rats of the control group (Figs. 5, 6 and 7).



Figs. 5, 6 and 7. — Prednisone group, Sudan staining. About 50 x.

Cortisone group. — The zona glomerulosa approximately corresponds to the foregoing groups in respect to stainability. The sudanophobic zone is also of the same width. The sudanophilic area of the zona fasciculata has generally narrowed considerably as compared to the prednisone and, especially, control groups. In part of the preparations the lipid content of the fascicular zone has decreased to a very large extent, while in others, again, sudanophilia is somewhat greater. The zona reticularis exhibits no appreciable sudanophilia. The thickness of the cortex as whole is smaller than that of the animals belonging to the prednisone group and, particularly, to the control group. The greatest individual variations in respect to both sudanophilia and the thickness of the cortex were observed in this group (Figs. 8, 9 and 10).



Figs. 8, 9 and 10. — Cortisone group, Sudan staining. About 50 x.

DISCUSSION

The tests described in the foregoing show that there occurs notably less atrophy of the suprarenal body as a consequence of administering prednisone than after a four times larger dose of cortisone of equal therapeutic effect. Coste et al.(3) observed that cortisone, hydrocortisone and prednisone caused the same kind of eosinopenic reaction. The result of our study shows that the side-effects attending the administration of cortisone and prednisone in the dosages used by us, are not the same on all the organs. The prednisone dose in question does not, perhaps, have quite so strong an inhibitory effect on the endogenic corticoid secretion, so one might consider that the suprarenal body in this event augments the anti-inflammatory effect through its own functioning. Cortisone administered as a fourfold dose evidently has a stronger inhibitory effect on ACTH secretion than prednisone. Since the changes in the suprarenal cortex are slighter after the administration of prednisone than cortisone, it may be assumed that the regeneration of the suprarenal cortex of animals receiving prednisone is also faster. Insofar as changes in the human suprarenal body correspond to those described in the foregoing in the case of laboratory animals, prednisone may be regarded as more advantageous in therapy than cortisone when changes to be met with in the suprarenal body are the criterion.

SUMMARY

The writers have investigated the effect of cortisone and prednisone on the suprarenal body of albino rats. As a result of the tests carried out, it was observed that a prednisone dose decreases the weight of a rat's suprarenal body significantly less than a cortisone dose of clinically the same strength. Sudan staining also made evident a notably slighter disappearance of lipids in the area of the fascicular zone after the administration of prednisone than of cortisone.

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